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REMARKS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claim 1 has been amended to introduce mainly editorial changes that are not believed to require anything other than a cursory review by the Examiner.

A couple of changes to claim 1 do, however, require explanation. First, in step c), the concept that markers are detected in a cell or in a constituent region of a section of the tissue sample can be taken from the fourth sentence of paragraph [0014] of US 2002/0123845.

Second, Applicants have specified in step d) that the combined and accredited signals are compared to a threshold value and this is used to indicate the presence of cancer cells or their precursors in the cell sample or tissue sample. This is supported by paragraphs [0016], [0045] and [0046] of US 2002/0123845.

New claim 9 is drawn to the detection of the markers in a cell.

New claim 10 is drawn to the detection of the markers in a section of the tissue sample.

Applicants respectfully submit that none of the changes introduce new matter. An early notice to that effect is earnestly solicited.

Claims 1-5, 7 and 8 were rejected under 35 USC § 112, second paragraph, as being indefinite. In response, Applicants have amended claim 1 in a manner that is believed to overcome the Examiner's concerns. Thus, Applicants have added the word "said" to step b) to make clear that the markers discussed there are the same markers mentioned in step a). Also, Applicants have amended step c) to make reference to "a section of said tissue sample" to obviate the need for antecedent basis for "tissue section."

In view of the foregoing, Applicants respectfully submit that the claims are now definite. An early notice to that effect is earnestly solicited.

Claims 1, 2, 4, 5 and 8 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3 and 4 of copending USSN 10/022,618. In response, Applicants respectfully request that this issue be held in abeyance until allowable subject matter is indicated, at which time Applicants will take appropriate action, for example, file a suitable terminal disclaimer or prove patentable distinctness.

Claims 1, 2 and 5 were rejected under 35 USC § 102(b) as being anticipated by Rao et al. ("Rao"), *Cancer Epidem. Biomarkers & Prevention*, 7: 1027-1033 (1998). In response, Applicants respectfully submit that Rao does not anticipate the present claims. According to the present claims, signal intensities from two or more markers are detected *within a single cell or within a constituent region of a section of a tissue sample (step c))* and then the signal intensities are combined and accredited and then *the combined and accredited signal intensities are compared to threshold values* to indicate the presence of cancer cells and their precursors in a cell sample or tissue sample (step d)). Rao contains no teaching of detecting

multiple markers within a single cell or within a constituent region of a tissue section, and of combining and accrediting the signal intensities detected, and of comparing the combined and accredited signal intensities to a threshold value to indicate the presence of cancer cells or their precursors in the cell sample or tissue sample. Therefore, Rao cannot anticipate the present claims.

Rao measures the intensity over the whole slide (see page 1029, right column, first sentence). This intensity is compared with the intensity of a slide with a known positive cell line (see page 1029, right column up to page 1030, left column). If the intensity for a marker over the whole slide is higher than the intensity of the comparison slide, then this case is scored positive. The pitfall of Rao is shown in Table 1 on page 1029. Samples 12 and 27 have no cancer but are found positive for two markers. On the other hand cancer Samples 46 and 55 only show a positive signal for just one marker.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 1, 3-5 and 8 were rejected under 35 USC § 102(b) as being anticipated by McNamara et al. ("McNamara"), US 6,007,996. In response, Applicants respectfully submit that McNamara suffers from the same defects as Rao. Thus, McNamara also does not teach detecting multiple markers within a single cell or within a constituent region of a tissue section, and combining and accrediting the signal intensities detected, and comparing the combined and accredited signal intensities to a threshold value to indicate the presence of

cancer cells or their precursors in the cell sample or tissue sample. Consequently, McNamara also cannot, as a matter of law, anticipate the present claims.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 7 was rejected under 35 USC § 103(a) as being obvious over Rao or McNamara in view of Bacus et al. ("Bacus"), US 5,109,429. In response, Applicants point out that this rejection was premised on Rao or McNamara anticipating claim 1, which has been shown above to be incorrect. Therefore, Applicants respectfully submit that this rejection should be reconsidered and withdrawn as well. Nothing in Bacus alone or in combination with either Rao or McNamara bridges the clear gaps between Rao or McNamara and the instant claims. Consequently, the combination of Rao or McNamara and Bacus does not make out a prima facie case of the obviousness of claim 7.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

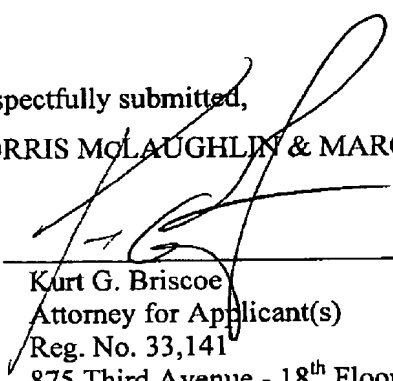
Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully

requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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